SYPHILIS OF THE NERVOUS SYSTEM IN SOME OF ITS CLINICAL AND PATHOLOGICAL MANIFESTATIONS.[1]

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It is my[2] opinion that in tabetic ocular palsies, as well as in those recognized as syphilitic ocular palsies, the lesion is not primarily nuclear but is in the nerve fibers as they leave the brain, and I have reported a case of tabes with intense ocular palsies in which the microscopic findings gave much lymphocytic infiltration of the ocular nerves. I am not prepared to state a conviction that primary nuclear palsy of the cranial nerves in tabes is impossible, but I do believe that most tabetic cranial nerve palsies are primarily radicular, and that when nuclear changes are found in tabes they occur in cases of long standing. It is to be expected that when nerves have been degenerated near their nuclear origin during a period of years the nerve cells from which these degenerated fibers arise should show alteration. This view-point is of therapeutic as well as pathological importance, for if the degeneration be in the nerve we may expect recovery from persistent antisyphilitic treatment, provided the degeneration be not too intense and the treatment be begun early; whereas we may expect much less improvement if the cells of origin be primarily affected.

There are cases in which syphilitic ocular palsy is not caused by basal meningitis but by softening implicating the nuclei or nerve fibers of the affected nerve, and a case of bilateral softening forming two separate foci in the oculomotor nuclei I[3] described in 1913.

It is well known that tabetic palsies often disappear, and this subject was discussed by Posey[4] in a symposium on the "Neuro-ocular Symptoms of Tabes" in April, 1915. He stated that it is an almost constant experience that the palsies that appear in the early stages of the disease vanish after periods of persistency ranging from but a few hours to two or three weeks; and while it is true that the palsies that occur in the later stages are, as a rule, permanent, even these may be transient and may totally disappear, usually after a longer period than when they are observed at the commencement of the disease.

Posey found that the palsies vanished for a time, at least in perhaps 90 per cent. of the cases which he had under observation.

[1] Read as part of a symposium on syphilis held at a meeting of the College of Physicians of Philadelphia, February 7, 1917.
[2] Spiller: Jour. Nerv. and Ment. Dis., January, 1915, p. 15.
[3] Spiller: Le Névraxe, 1913, xiv.
[4] Pennsylvania Med. Jour., October, 1915, p. 55; Jour. Am. Med. Assn., April 16, 1910.

This percentage was based on an analysis of the history of 60 cases taken from his own records and from the study of 28 cases of advanced tabes which he had at one time made in the wards of the Philadelphia General Hospital.

The tendency of the palsies to recur was also dwelt upon, either the same muscles being repeatedly palsied or the paralysis appearing in one or more muscles shortly after it had disappeared in a muscle governed by the same nerve. In some cases the palsy may pass away in a few hours; in others it may persist for years. This return of the muscle to its normal even after years of paralysis he thought should be recognized by ophthalmic surgeons, and should tend to discontinue operations on the eye muscles of tabetics. Tabetic palsies are usually dissociated. This is essentially true when the palsy appears as an initial symptom.

It is important to determine how long an ocular palsy in cerebral syphilis may persist and yet have a final recovery. An interesting case from this point of view is the following: Oscar T., aged thirty-two years, was referred from Dr. de Schweinitz's service April 11, 1914, to the neurological department of the University of Pennsylvania with the note: "Complete palsy of the left external rectus muscle; pupils 3 mm.; no fundus changes; light reaction of pupils gone; faint convergence reaction."

The man contracted syphilis at the age of twenty years.

The symptoms began three weeks before he came to the hospital, with dizziness, and this was soon followed by rapidly developing diplopia. He had headache of moderate intensity, tinnitus in the right ear, paresthesia in the lower limbs, and a sense of constriction about the knees. Station and gait were normal. The patellar reflexes were normal, but the Achilles reflexes were lost. He had no disturbance of the bladder and no disturbance of sensation, even in the distribution of the lower sacral roots. Slight outward rotation of the left eyeball was observed May 6, 1914.

The next note made was on December 24, 1914: "Ocular palsy seems less than it was eight months ago." He was taken into the hospital on this date. He had diminution of pain sensation in the first and second divisions of the right fifth nerve. On December 29 Dr. Langdon reported: "Central vision normal in each eye and fields of vision normal for form and color, although disks show some pallor in temporal portion. No other fundus changes. O. D. pupil 4 mm. O. S. 3.5 mm. Both Argyll Robertson."

Dr. Butler found the hearing apparently normal.

The Wassermann reaction was negative. He was given the protiodide of mercury, gr. $\frac{1}{4}$.

February 14 and 15 the note was made that the motion in the left eye was gradually returning. February 24 the external rectus palsy had almost disappeared. March 4, Dr. de Schweinitz found concomitant squint was about 15 degrees; the left external rectus

now moved the eye to the outward commissure by 33-degree prism base out.

Slight improvement began soon after the patient first came under observation, but the restoration had not amounted to much ten months after the onset of the palsy, although the man had been treated for syphilis at another hospital. Then the improvement advanced rapidly. At the present time there is only slight ocular palsy.

Another case of long-standing ocular palsy with final recovery occurred under the observation of Dr. de Schweinitz, as shown in a letter from him March 5, 1915: "Referring to our conversation in regard to the recovery of long-standing palsies of the exterior ocular muscles, I have to say that the patient concerning whom I spoke to you is a woman, aged fifty-eight years, whose eyes I have known since the middle of November, 1892, correcting them at stated intervals for a varying hyperopic astigmatism. February 24, 1914, she came with a history of three weeks of diplopia and much left-sided neuralgic pain. She was excessively nervous; there were no nasopharyngeal troubles; no history of rheumatism. Urine examination was negative, but both the Wassermann and the Noguchi reactions were positive, the examination having been made by Dr. Corson White. The left external rectus was the muscle involved, and no other exterior ocular muscle was affected. The palsy was not quite complete, and the diplopia neutralized by a 25- to 30-degree prism base out. I knew that she had been under the care of a man who has a sanitarium, and asked him for some data. He tells me under date of April 18, 1914, that five years previously she had been under his care in his sanitarium because 'her family feared insanity.' He then goes on to say: 'I found no signs of mental unsoundness, and the patient recovered rapidly in about a month's time. I ascribed her condition at that time to the nervous phenomena which follow the menopause.' This paresis of the left abducens remained practically stationary; in point of fact, for the first few days it increased so that there was practically no movement outward. I say 'practically' there was, perhaps, 1 mm. of movement on strong efforts at abduction, and the diplopia could be with difficulty neutralized with very high prisms between 40 and 50 degrees. At first a mixture of iodide of sodium and aspirin was tried. This was soon stopped and iodide of potassium and bichloride of mercury were ordered. There was practically no improvement until about the middle of August of the same year—that is, six months after treatment was begun—when the diplopia became less marked, the neutralization first requiring between 25 and 30 degrees of prism and then between 15 and 20 degrees, and the movement of the eye was slightly improved, the first record of increased movement being on August 12, 1914. During all this period of time, with the exception of the first week, she took very large doses of iodide

of potassium, never less than 90 grains a day, and sometimes as much as 100 grains a day. Between August 12 and December 9 the diplopia remained practically stationary, neutralized by a 15- to 18-degree prism. Indeed, this condition of affairs did not alter materially, maybe only 2 or 3 degrees, until January 7 of this year, when the diplopia had dropped to 7 degrees, and at the last examination, on April 10, was not noticeable, although it could be developed by a red glass, and the movement of the eye was practically normal."

The cause of such palsy, as already said, is usually basal syphilitic meningitis, as illustrated in the following case, which is like the one described by me in 1915:

J. H., aged fifty years, entered the service of Dr. Solis Cohen November 17, 1914, having pneumonia, and died November 29, 1914. He was delirious and consequently a thorough examination could not be made. He had ptosis of the right upper eyelid, the pupils were unequal, and the right was larger and did not react to light. There was obliteration of the lines of expression. In May, 1914 the note was made that he had partial ptosis of the right upper eyelid, the right pupil was larger than the left and irregular, and did not react to light or in accommodation. The right eyeball was rotated outward. He had almost a complete right oculomotor palsy, as he had very slight movement of the right eyeball inward, upward or downward. The left iris did not react to light but did in convergence. The movements of the left eyeball were normal. The oculomotor palsy had developed rapidly a year and a half previously. He was able to count fingers readily with either eye, and examination of the eye-grounds revealed nothing abnormal. He was brought to the hospital because of the ocular condition. He did not comprehend questions readily, was somewhat confused as to time and place, and his memory was feeble. The patellar reflexes were absent.

The microscopic examination in serial sections of the cerebral peduncles showed moderate infiltration of mononuclear cells in the pia at the exit of the oculomotor nerves and disappearance of many nerve cells in the oculomotor nuclei. The origin of the ocular palsy was probably the syphilitic basal meningitis. The posterior columns in the lower part of the medulla oblongata were degenerated as in tabes, and the case was evidently one of tabes, although the spinal cord was not obtained.

Stargardt[1] investigated the causes of optic atrophy in tabes and paresis in 25 cases, and examined the visual system from the external geniculate body to the retina. When the optic nerve was normal the retina also was normal. Where changes occurred in the retina they were secondary to changes in the optic nerve and differed in no way from those observed after division of the optic nerve or

[1] Allg. Ztschr. f. Psychiat., 1912, lxix, 735.

compression of this nerve by a sclerotic internal carotid artery. The cause of the optic atrophy was exudative processes in the chiasm and the intracranial portion of the optic nerves. The optic tract and external geniculate body showed only secondary degeneration. In cases of partial optic atrophy the atrophy was the result of partial infiltration of the intracranial portion of the optic nerve. He concludes that there was no ascending atrophy from any intoxication of the ganglion cells of the retina, as has been assumed. In all cases of optic atrophy he found infiltrative processes in the parts about the chiasm and the optic nerves. The changes in the optic nerves therefore resemble those in the nerves supplying ocular muscles.

It has been my custom for years in studying syphilis of the brain in the laboratory to examine especially the cerebral peduncles and optic chiasm, because if there are manifestations of syphilis in the brain it is here especially we may expect to find lesions. It is because this region of the brain is specially liable to be affected by syphilitic lesions that syphilis may cause the symptoms of tumor of the pituitary body.

I have seen several cases of complete bilateral isolated paralysis of the seventh nerve in syphilis with recovery, and two such cases observed in my service are reported in a paper by Harvey W. Ewing.[6] The lesion must be an infiltration of mononuclear cells in the pia, but it is indeed strange that two nerves of similar distribution, but remote from one another in origin, should alone be picked out by the syphilitic lesion. I have also seen implication of the fifth nerve alone, and reported such a case with necropsy with Camp.

It is desirable to remember that permanent results were accomplished in the treatment of nervous syphilis in some cases before the days of salvarsan and the modern laboratory methods of investigation. Unfortunately, we must confess that our modern methods, while usually of great value, are not satisfactory in all cases of nervous syphilis, and that some cases do not respond to any treatment, and others may respond and then relapse. I have had the opportunity recently to reëxamine a man who, in 1897, was in the service of Dr. James Hendrie Lloyd[7] at the Philadelphia General Hospital, and whose case was reported by Dr. Lloyd at that time.

The man then was twenty-one years of age, and had a history of syphilis. His symptoms of syphilitic disease of the nervous system were pronounced, and he improved greatly under the administration of mercury, and possibly iodide, and has remained in this improved condition during nineteen years. At present this man is in very fair condition; he has gained flesh, and aside from his polyuria and third nerve palsy, which he has had since 1897, he has few signs of disease. He is employed as a workman in the Philadelphia General Hospital.

[6] Jour. Am. Med. Assn., May 9, 1914.

[7] Diseases of the Cerebrospinal and Sympathetic Nerves, Twentieth Century Practice.

I am unable to obtain any information that salvarsan or neosalvarsan had even been used in his treatment, and certainly his improvement and present condition were obtained before the recent methods of treatment were discovered, and there has been no serious relapse during a long period of years.

Syphilis affects not only the outer covering of the brain but also the lining of the ventricular spaces, and may produce intense lesions here. Proliferations of the ependyma may be great, and the aqueduct may be occluded in the same way as frequently is one of the brain arteries, and in this manner hydrocephalus may result. I have observed hydrocephalus confined to one posterior horn of a lateral ventricle or confined to the lateral ventricle of one cerebral hemisphere. A recent case in which hydrocephalus was confined to the posterior horn of one lateral ventricle occurred in the service of Dr. Mills. In studying the cause of this enlargement I found that syphilitic adhesions had formed in the middle of the ventricle, blocking off the posterior horn from the remaining ventricles.

W. H. entered the hospital June 10, 1913. He had been having left-sided headaches for six weeks, but had had right-sided convulsions nineteen years. The right retina was slightly swollen and the arteries were smaller than normal. The right field for white was slightly contracted. The left iris reacted very slightly to light; the left retina was swollen so as to make the edges of the vessels not so well defined as normal. The arteries were small, the veins larger than in the right eye. The left field for white was greatly contracted.

In July, 1913, left-sided symptoms had developed. Saliva dribbled from the left corner of the mouth, and the left side of the face showed paralysis, the left upper limb was weaker than the right, and patellar and Achilles reflexes were prompter on the left side, and the gait was that of left hemiparesis.

Dr. Holloway, about July 11, 1913, found there was no hemianopsia, but there was a tendency for deviation of the eyes to the right. It would seem as though this might have been because of defective vision in the right fields, especially as the patient's condition was such that accurate visual tests could not be made. Death followed an operation on the head. The necropsy was made July 24, 1913.

The examination showed much lymphocytic infiltration of the pia about the optic chiasm and at the base of the brain. The posterior and inferior horns of the left lateral ventricle were much dilated, but the anterior horn of this ventricle was of normal size. The right lateral ventricle was normal. Adhesions in the left lateral ventricle near the foramen of Monro doubtless were the cause of the occlusion of the posterior horn of this ventricle, and probably were of syphilitic origin. An area of softening was found in the outer part of the right lenticular nucleus extending into the brain upward, and probably was the cause of the left-sided symptoms of late develop-

ment. The cortex about the outer part of the dilated left posterior horn was not over 2 mm. in thickness at its narrowest part, and it is difficult to understand why right lateral homonymous hemianopsia was not produced.

Considerable infiltration of mononuclear cells in the pia of the medulla oblongata and chiasm and thickening of the vessels in the pia of the chiasm were found.

There are cases of syphilis with intense infiltration of mononuclear cells in the pia, such as is the common finding in nervous syphilis, and yet the clinical manifestations cannot be distinguished from those of tabes. Such a case is the following: A man, W. F. P., aged sixty-one years, was in my service at the Philadelphia General Hospital, and died there in 1911. He had a chancre when nineteen years old. About twenty years before he came under my observation his symptoms began with severe shooting pains in the lower limbs, and he became obliged to use a cane in walking. His eyesight began to fail about fifteen years before his admission to the hospital, and in about seven years he became blind. He had dribbling of urine. The Wassermann reaction of the blood was positive. The irides did not react to light, but did in convergence. He had loss of patellar reflexes, ataxic gait, diminution of touch and pain sensations, gastric crises, etc. It is not surprising that others as well as I regarded this case as a typical one of tabes.

The findings were intense infiltration of mononuclear cells in the pia of the spinal cord and of the chiasm and optic nerves, as well as of the chiasm itself. The optic nerves were intensely degenerated. Degeneration was seen in the posterior columns of the cord.

In tabes, as a rule, the infiltration of mononuclear cells in the spinal pia is slight, but death usually occurs late in the disease, and it is possible that the infiltration may have been pronounced in the early stage of the disease.

Of much clinical and pathological significance is the association of syphilis of the central nervous system with other lesions of this part entirely independent of the syphilitic process. I have reported a case in which I had made the diagnosis from the symptoms of tabes associated with syringomyelia, and the necropsy confirmed this diagnosis. A similar case had previously been reported by Schlesinger.

Recently, I[8] reported at a meeting of the Philadelphia Neurological Society a case in which the lesions of grave anemia of the spinal cord were associated with those of tabes.

In a symposium held at a meeting of the Philadelphia County Medical Society, September 27, 1916, I referred to the probability of certain cases of epilepsy having an origin in congenital syphilis, and mentioned that the examination of the family of a patient may

[8] Spiller: Pennsylvania Med. Jour., November, 1916, p. 128.

indicate that the patient probably has congenital syphilis. I think it is well to repeat here verbatim the words used on this subject at that meeting. A brief report of this symposium has been published:

"Probably no one will dispute that syphilis may produce epilepsy, but there are some cases of epilepsy in which syphilis may only be suspected and not proved. I refer to cases in which a father has had a chancre before the birth of his child and the child becomes epileptic. Such a case has recently come under my observation. A man, aged twenty-seven years, has been epileptic since the age of seventeen years, and no cause can be determined. He had no convulsions in childhood, no severe head trauma, but the statement is made by the father that he had an initial lesion about twenty-three years before the birth of the son. The son shows no evidence of syphilis, his blood Wassermann is negative, and yet congenital syphilis may be the cause of the epilepsy. An elder brother had the notched teeth of hereditary syphilis."

Stoll[9] has published recently an interesting paper on "Hereditary Syphilis as a Cause of Chronic Invalidism," and states he judges that the diagnosis of hereditary syphilis by intensive familial study is not generally practised, as no mention was made of it in four symposiums which he recently attended in which many well-known syphilologists discussed the various problems of syphilis.

The subject of syphilis is a broad one, and many interesting features of this disease must of necessity be omitted in every symposium. I do not doubt that if the importance of family infection had been mentioned in these symposiums much information would have been forthcoming. It is certainly not rare for a physician to examine the near blood relatives of a patient with either congenital or acquired syphilis. Much has been written on congenital syphilis, and one would be remiss in his examination if in a case of suspected congenital syphilis he failed to investigate the patient's family.

Epilepsy is definitely caused at times by acquired syphilis, and it may be possible to trace the relation of cause and effect. In other instances of epilepsy the syphilis remains unrecognized. The Wassermann reaction may be negative, as it frequently is, when syphilis of the nervous system is of very chronic type. The following case, occurring recently in my practice, is illustrative of this point of view. A man, aged thirty years, began to have epileptic attacks at the age of twenty-five years, in the form of petit mal occurring at long intervals. Six brothers and sisters of the man were healthy, and there was no epilepsy in the family. He had been much exposed to syphilis, but had no knowledge of venereal disease. The Wassermann test of the blood was negative. In examining this man for symptoms of organic disease I found that he had delayed mic-

[9] Jour. Am. Med. Assn., December 23, 1916.

turition; for a long time he had been unable to pass the urine unless the desire was very great, and he would stand for two to five minutes waiting for the urine to flow; he had lost sexual desire. The biceps and triceps reflexes were absent on both sides, the left patellar tendon reflex was very feeble, the right almost lost, and the Achilles reflexes were very weak.

There was not enough here to justify a diagnosis of syphilis, but there was enough to arouse a suspicion of this disease, and I urged the investigation of the spinal fluid and the cautious administration of mercury should the laboratory findings of the fluid be positive or even negative, because the infrequency of the attacks indicated a very chronic process compatible with negative laboratory findings.

It is often stated that syphilis of the central nervous system is a diffuse process implicating both brain and spinal cord. This usually is a correct statement. In a discussion on syphilis at the last meeting of the Congress of Physicians and Surgeons in Washington I called attention to the occurrence of focal syphilis of the central nervous system, in which the symptoms indicate that the lesion is confined to a very limited area. One of the most striking examples of this is a case of focal myelitis reported by me[10] in September, 1908. At that time we did not have the laboratory technic for the detection of syphilis we now possess. The occurrence of frequent attacks of "rheumatic pains," especially in the lower limbs, inequality of the pupils, loss of pupillary reaction, and a miscarriage at the fourth month suggest syphilis.

The case was one of hemiplegia. The muscles of the neck were rigid and voluntary movement of the neck was greatly impaired. Pain in the neck had been present about five weeks. Paralysis and rigidity of the muscles of the neck in hemiplegia are very extraordinary.

Microscopic examination showed small hemorrhages and swollen axis-cylinders in the third cervical segment. The small vessels in the cord had greatly thickened walls. Lymphocytic infiltration was found within the cord, and the nerve cells of the anterior horns were altered. The cord was less severely affected at the fourth cervical segment, and was about normal at the fifth cervical segment.

Usually when syphilis appears to be focal, careful examination will show further evidence of the disease, as in the two following cases:

Mrs. S., in September, 1915, complained of pain in the left buttock and left groin, and this pain became sharp and shooting in the left thigh. In March, 1916, the left lower limb began to be weak. In June, 1916, pain was noticed in the right lower limb, and at that time there was some rectal and vesical incontinence. When examined in July, 1916, the thighs and legs were distinctly wasted,

[10] Spiller: Jour. Nerv. and Ment. Dis., September, 1908.

the right lower limb could be raised easily from the bed, but the left limb could not be raised from the bed or flexed at the knee, although movement of the toes was retained. Passive flexion of the left knee caused great pain. Sense of position was much impaired in the toes of each foot. Tactile, pain, heat, and cold sensations were almost lost in the distribution of the left first and second lumbar roots, and were diminished in the distribution of the twelfth thoracic and third lumbar roots. The patellar reflex was diminished on the left side and increased on the right side. Persistent ankle-clonus was present on each side. Lumbar puncture yielded a light green fluid, coagulating within two or three minutes, as in the Nonne-Froin syndrome. The cell count was 5. The blood Wassermann was strongly positive.

The symptoms-complex was clearly that of a lesion on the left side of the lumbar cord, implicating the 12th thoracic and the 1st, 2d, 3d, and 4th lumbar roots, and later the right side of the cord, probably by pressure. On account of the focal character of the symptoms I requested Dr. Frazier to perform an exploratory operation, and this he did. The dura showed a white opacity at the level of the first lumbar vertebra, and the tension was considerable, and the cord at this region was enlarged. The operation caused a complete cessation of the pains in the lower limbs.

In December, 1916, the woman was able to flex and extend the left lower limb, partially at the knee; both patellar reflexes were slightly exaggerated, and there was much more power in the left lower limb than there had been before the operation. She had received antisyphilitic treatment.

While so far this appears as a sharply focalized syphilitic lesion, information was elicited that before the symptoms began in the lower limbs there had been pains of short duration in the upper part of the left upper limb and in the left chest. This indicated that the process was a diffuse one.

In another case the patient, Mrs. P., about two years previously began to have sharp pains in the anterior part of the left thigh, and in about two months this pain yielded to numbness in this region. There had been also some numbness in the right hip. The patellar reflex was absent on the left side and diminished on the right side. The Achilles tendon reflex was absent on each side. Touch, pain, heat and cold sensations were lost in the anterior part of the left thigh. The blood Wassermann was strongly positive.

Here also was a case of focal syphilis, similar to that in the case just recorded, but further examination showed that headache had been severe, that diplopia and ocular palsy were present, and that paresthesia existed in the lower lip.